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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,185	07/18/2001	C. Frank Bennett	RTS-0258	1505
7590 04/20/2004			EXAMINER	
Jane Massey Licata Licata & Tyrrell, P.C. 66 East Main Street Marlton, NJ 08053			ZARA, JANE J	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/910,185

Applicant(s)

BENNETT ET AL.

Examiner

Jane Zara

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

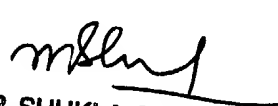
Claim(s) allowed: none.

Claim(s) objected to: none.

Claim(s) rejected: 1,2,4-10, 12-15.

Claim(s) withdrawn from consideration: none.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

  
**RAM R. SHUKLA, PH.D.**  
**PRIMARY EXAMINER**

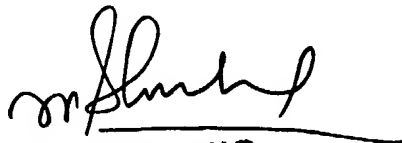
Attachment

Applicants argue that the instant 102 and 103 rejections do not properly apply as prior art for various reasons. Applicants argue that the antisense primers taught by Kalff-Suske et al and applied as 102 art against claims 1 and 2 of the instant application do not specifically hybridize to glioma associated oncogene 3 of SEQ ID NO: 3 because Kalff-Suske teach mutations directly involved in various conditions associate with aberrant expression of glioma associated oncogene 3. Contrary to Applicants' assertions, the antisense disclosed by Kalff-Suske et al, despite the major emphasis of the article, are antisense oligonucleotides that specifically hybridize and inhibit the expression of glioma associated oncogene 3 in vitro. Whether they were used for other uses (such as PCR amplification) or not does not alter their ability to specifically hybridize to the target gene glioma associated oncogene 3. And absent evidence to the contrary, the phosphorylated form of these antisense oligonucleotides also retain the ability to specifically hybridize to the target gene and inhibit its expression in vitro.

Applicants argue that the 103 rejection is improper because Ruppert and Kalff-Suske do not specifically disclose the inhibition of the target gene glioma associated oncogene 3 in vitro using antisense. Contrary to Applicants' assertions, both Ruppert and Kalff-Suske provide the nucleotide sequence of the target glioma associated oncogene 3 gene, as well as the motivation to inhibit its expression because of its involvement in various pathological conditions. Ruppert and Kalff-Suske both provide the polynucleotide sequence that enable the motivated artist of ordinary skill in the art to

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design and assess antisense oligonucleotides in their ability to inhibit the expression of glioma associated oncogene 3 in vitro. This general methodology was taught previously by Milner for any previously characterized target gene of interest and therefore, contrary to Applicants' assertions, it was routine to utilize the general technique taught by Milner, and used routinely by others in the field of antisense, to design antisense oligonucleotides and test them for their ability to inhibit the expression of glioma associated oncogene 3 in vitro. Furthermore, it would be reasonably expected that, knowing the target gene's nucleotide sequence, and knowing the routine experimental procedures taught by Milner to test the ability of any antisense to target and inhibit the expression of any target gene in vitro, candidate antisense oligonucleotides are routinely found that successfully inhibit the target gene's expression in vitro. Therefore, one of ordinary skill in the art would have been motivated to target and inhibit glioma associated oncogene 3 expression because of this oncogene's involvement in various cellular anomalies, and one of ordinary skill in the art would have reasonably expected to design, test and identify antisense that specifically target and inhibit this target gene's expression in vitro using the routine techniques described in the Milner reference.

  
**RAM R. SHUKLA, PH.D.**  
**PRIMARY EXAMINER**